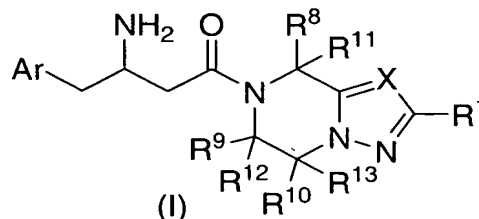


WHAT IS CLAIMED IS:

1. A compound of the formula I:



or a pharmaceutically acceptable salt thereof; wherein

each n is independently 0, 1, or 2;

X is N or CR²;

- 10 Ar is phenyl substituted with one to five R³ substituents;

R¹ and R² are each independently selected from the group consisting of

hydrogen,

halogen,

15 cyano,

C₁₋₁₀ alkyl, wherein alkyl is unsubstituted or substituted with one to five

halogens,

C₁₋₁₀ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five substituents

independently selected from halogen or hydroxy,

20 C₁₋₁₀ alkylthio, wherein alkylthio is unsubstituted or substituted with one to five

substituents independently selected from halogen or hydroxy,

C₂₋₁₀ alkenyl, wherein alkenyl is unsubstituted or substituted with one to five

substituents independently selected from halogen or hydroxy,

(CH₂)_nCOOH,

25 (CH₂)_nCOOC₁₋₆ alkyl,

(CH₂)_nCONR⁴R⁵, wherein R⁴ and R⁵ are independently selected from the group

consisting of hydrogen, tetrazolyl, thiazolyl, (CH₂)_n-phenyl, (CH₂)_n-C₃₋₆

cycloalkyl, and C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one

to five halogens and wherein phenyl and cycloalkyl are unsubstituted or

30 substituted with one to five substituents independently selected from halogen,

hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

or R⁴ and R⁵ together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

(CH₂)_n-NR⁴R⁵,

(CH₂)_n-OCONR⁴R⁵,

(CH₂)_n-SO₂NR⁴R⁵,

(CH₂)_n-SO₂R⁶,

(CH₂)_n-NR⁷SO₂R⁶,

(CH₂)_n-NR⁷CONR⁴R⁵,

(CH₂)_n-NR⁷COR⁷,

(CH₂)_n-NR⁷CO₂R⁶,

(CH₂)_n-COR⁶,

(CH₂)_n-aryl, wherein aryl is unsubstituted or substituted with one to five substituents independently selected from halogen, CN, hydroxy, NR⁷SO₂R⁶, SO₂R⁶, CO₂H, C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkyl and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five substituents independently selected from halogen, CO₂H, and C₁₋₆ alkyloxycarbonyl,

(CH₂)_n-heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

(CH₂)_n-heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

(CH₂)_n-C₃₋₆ cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and

wherein any methylene (CH₂) carbon atom in R¹ or R² is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl unsubstituted or substituted with one to five halogens;

- 5 each R³ is independently selected from the group consisting of
hydrogen,
halogen,
cyano,
hydroxy,
10 C₁₋₆ alkyl, unsubstituted or substituted with one to five halogens, and
C₁₋₆ alkoxy, unsubstituted or substituted with one to five halogens;

- R⁶ is independently selected from the group consisting of tetrazolyl, thiazolyl, (CH₂)_n-phenyl, (CH₂)_n-C₃₋₆ cycloalkyl, and C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one
15 to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, and wherein any methylene (CH₂) carbon atom in R⁶ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, C₁₋₄ alkyl, and C₁₋₄ alkoxy, wherein alkyl and
20 alkoxy are unsubstituted or substituted with one to five halogens;

each R⁷ is hydrogen or R⁶;

- R⁸, R⁹, R¹⁰, R¹¹, R¹², and R¹³ are each independently selected from the group consisting of:
25 hydrogen,
cyano,
(CH₂)_nCOOH,
(CH₂)_nCOOC₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to three
substituents independently selected from halogen and phenyl,
30 C₁₋₁₀ alkyl, unsubstituted or substituted with one to five substituents independently
selected from halogen, hydroxy, C₁₋₆ alkoxy, carboxy,
C₁₋₆ alkyloxycarbonyl, and phenyl-C₁₋₃ alkoxy, wherein alkoxy is unsubstituted
or substituted with one to five halogens,
(CH₂)_n-aryl, wherein aryl is unsubstituted or substituted with one to five substituents
35 independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy,

wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

(CH₂)_n-heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

(CH₂)_n-heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

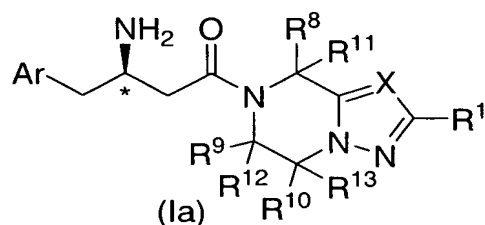
(CH₂)_n-C₃₋₆ cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

(CH₂)_nCONR⁴R⁵, wherein R⁴ and R⁵ are independently selected from the group consisting of hydrogen, tetrazolyl, thiazolyl, (CH₂)_n-phenyl, (CH₂)_n-C₃₋₆ cycloalkyl, and C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

or wherein R⁴ and R⁵ together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and

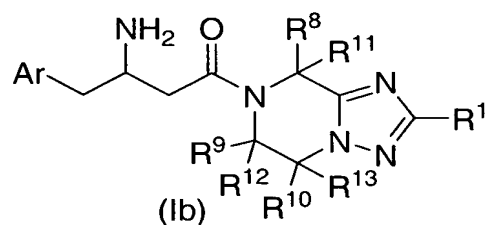
wherein any methylene (CH₂) carbon atom in R⁸, R⁹, R¹⁰, R¹¹, R¹², or R¹³ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl unsubstituted or substituted with one to five halogens.

2. The compound of Claim 1 of the formula Ia:



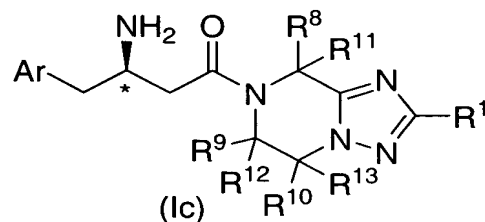
wherein the carbon atom marked with an * has the *R* configuration and Ar, X, R¹, R⁸, R⁹, R¹⁰, R¹¹, R¹², and R¹³ are as defined in Claim 1.

- 5 3. The compound of Claim 1 of the formula Ib:



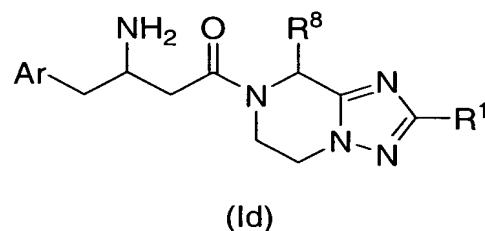
wherein Ar, R¹, R⁸, R⁹, R¹⁰, R¹¹, R¹², and R¹³ are as defined in Claim 1.

4. The compound of Claim 3 of the formula Ic:



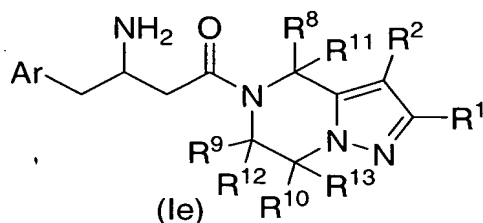
wherein the carbon atom marked with an * has the *R* configuration and Ar, R¹, R⁸, R⁹, R¹⁰, R¹¹, R¹², and R¹³ are as defined in Claim 1.

5. The compound of Claim 3 of the formula Id:



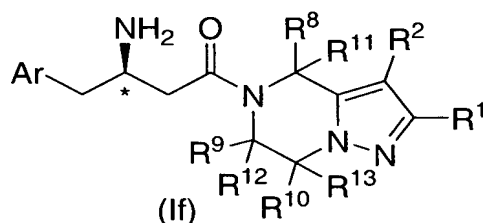
wherein Ar, R¹, and R⁸ are as defined in Claim 1.

6. The compound of Claim 1 of the formula Ie:



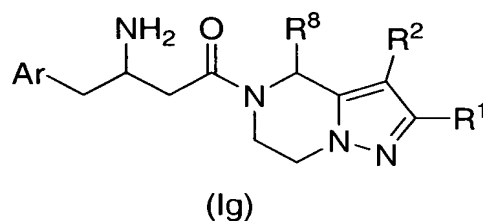
5 wherein Ar, R¹, R², R⁸, R⁹, R¹⁰, R¹¹, R¹², and R¹³ are as defined in Claim 1.

7. The compound of Claim 6 of the formula If:



10 wherein the carbon atom marked with an * has the *R* configuration and Ar, R¹, R², R⁸, R⁹, R¹⁰, R¹¹, R¹², and R¹³ are as defined in Claim 1.

8. The compound of Claim 6 of the formula Ig:



15 wherein Ar, R¹, R², and R⁸ are as defined in Claim 1.

9. The compound of Claim 1 wherein R³ is selected from the group consisting of hydrogen, fluoro, chloro, bromo, trifluoromethyl, and methyl.

20 10. The compound of Claim 9 wherein R³ is selected from the group consisting of hydrogen, fluoro, and chloro.

11. The compound of Claim 10 wherein R^3 is hydrogen or fluoro.

12. The compound of Claim 1 wherein R^1 is selected from the group
5 consisting of:

hydrogen,

C_{1-6} alkyl, wherein alkyl is unsubstituted or substituted with one to five fluorines,

$(CH_2)_n$ -phenyl wherein phenyl is unsubstituted or substituted with one to five

substituents independently selected from hydroxy, halogen, C_{1-6} alkyl, C_{1-6}

10 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five
halogens,

C_{3-6} cycloalkyl, unsubstituted or substituted with one to five substituents independently
selected from halogen, hydroxy, C_{1-6} alkyl, and C_{1-6} alkoxy, wherein alkyl and

alkoxy are unsubstituted or substituted with one to five halogens; and

15 wherein any methylene (CH_2) carbon atom in R^1 is unsubstituted or substituted with one to two
groups independently selected from halogen, hydroxy, and C_{1-4} alkyl unsubstituted or
substituted with one to five halogens.

13. The compound of Claim 12 wherein R^1 is selected from the group
20 consisting of

hydrogen,

methyl,

ethyl,

difluoromethyl,

25 trifluoromethyl,

CH_2CF_3 ,

CF_2CF_3 ,

phenyl, and

cyclopropyl.

14. The compound of Claim 13 wherein R^1 is selected from the group
consisting of hydrogen, difluoromethyl, trifluoromethyl, phenyl, and cyclopropyl.

15. The compound of Claim 1 wherein R^2 is selected from the group
35 consisting of

hydrogen,
 C₁₋₆ alkyl, unsubstituted or substituted with one to five fluorines,
 phenyl, unsubstituted or substituted with one to three substituents independently selected
 from fluoro, chloro, trifluoromethyl, methoxy, and OCF₃, and
 5 C₃₋₆ cycloalkyl, unsubstituted or substituted with one to five substituents independently
 selected from halogen, hydroxy, C₁₋₆ alkyl, and
 C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one
 to five halogens.

10 16. The compound of Claim 15 wherein R² is selected from the group
 consisting of hydrogen, trifluoromethyl, phenyl, and cyclopropyl.

17. The compound of Claim 16 wherein R² is hydrogen or trifluoromethyl.

15 18. The compound of Claim 1 wherein R¹¹, R¹², and R¹³ are each hydrogen
 and R⁸, R⁹, and R¹⁰ are each independently selected from the group consisting of:

hydrogen,
 C₁₋₆ alkyl, unsubstituted or substituted with one to five substituents independently
 selected from halogen, hydroxy, C₁₋₆ alkoxy, and phenyl-C₁₋₃ alkoxy, wherein
 20 alkoxy is unsubstituted or substituted with one to five halogens,
 (CH₂)_nCOOH,
 (CH₂)_nCOOC₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to three
 substituents independently selected from halogen and phenyl,
 (CH₂)_nCONR⁴R⁵, wherein R⁴ and R⁵ are independently selected from the group
 25 consisting of hydrogen, tetrazolyl, thiazolyl, (CH₂)_n-phenyl, (CH₂)_n-C₃₋₆
 cycloalkyl, and C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one
 to five halogens and wherein phenyl and cycloalkyl are unsubstituted or
 substituted with one to five substituents independently selected from halogen,
 hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted
 30 or substituted with one to five halogens;
 or wherein R⁴ and R⁵ together with the nitrogen atom to which they are attached
 form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine,
 piperazine and morpholine wherein said heterocyclic ring is unsubstituted or
 substituted with one to five substituents independently selected from halogen,

hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,
 (CH₂)_n-phenyl, wherein phenyl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,
 (CH₂)_n-heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,
 (CH₂)_n-heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,
 (CH₂)_n-C₃₋₆ cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are optionally substituted with one to five halogens; and
 wherein any methylene (CH₂) carbon atom in R⁸, R⁹ or R¹⁰ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl unsubstituted or substituted with one to five halogens.

19. The compound of Claim 18 wherein R⁸, R⁹, and R¹⁰ are each independently selected from the group consisting of:

hydrogen,
 C₁₋₃ alkyl, unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C₁₋₆ alkoxy, and phenyl-C₁₋₃ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,
 (CH₂)_nCOOH,
 (CH₂)_nCOOC₁₋₆ alkyl, wherein alkyl is unsubstituted or phenyl,
 (CH₂)_nCONR⁴R⁵, wherein R⁴ and R⁵ are independently selected from the group consisting of hydrogen and C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens;
 or wherein R⁴ and R⁵ together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine,

piperazine and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

(CH₂)_n-phenyl, wherein phenyl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

(CH₂)_n-heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are optionally substituted with one to five halogens,

(CH₂)_n-heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are optionally substituted with one to five halogens,

(CH₂)_n-C₃₋₆ cyclopropyl; and

wherein any methylene (CH₂) carbon atom in R⁸, R⁹ or R¹⁰ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl unsubstituted or substituted with one to five halogens.

20. The compound of Claim 19 wherein R⁸, R⁹, and R¹⁰ are each independently selected from the group consisting of:

hydrogen,

CH₃,

CH₂CH₃,

CH₂-cyclopropyl,

CHF-cyclopropyl,

CH(OH)-cyclopropyl,

CH₂OCH₂Ph,

CH₂(4-F-Ph),

CH₂(4-CF₃-Ph),

CH₂-[1,2,4]triazol-4-yl,

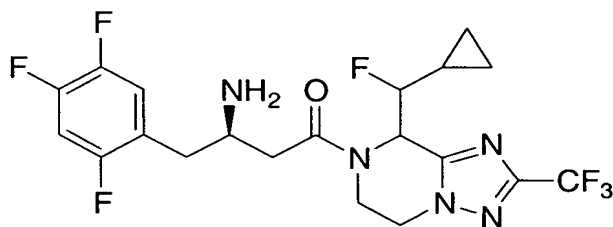
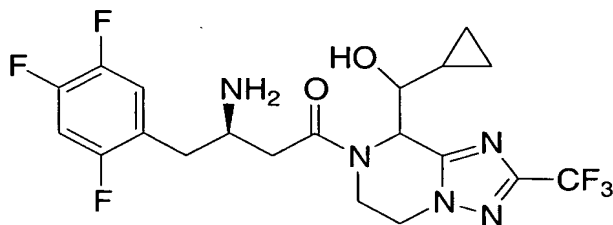
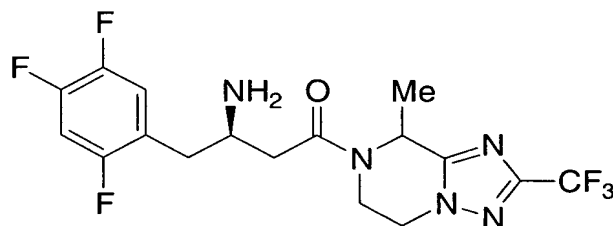
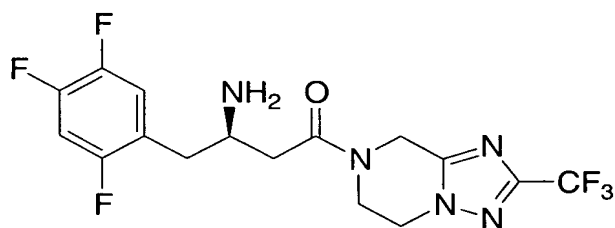
CH₂-(imidazol-1-yl),

CH₂-(pyrazol-1-yl),

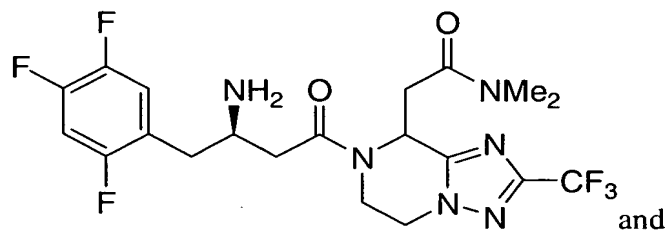
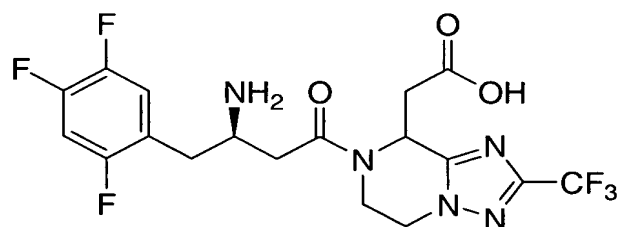
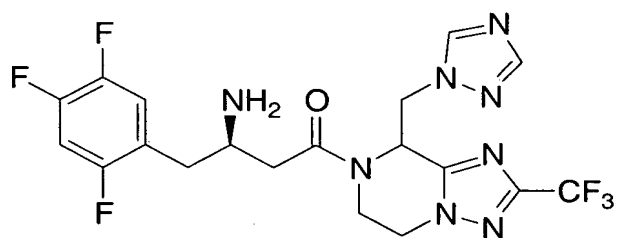
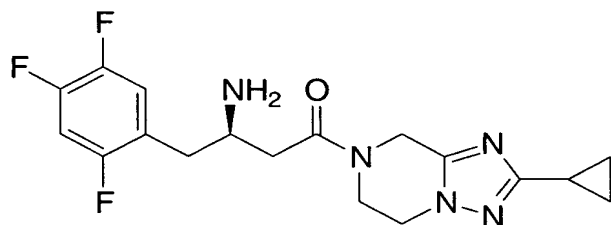
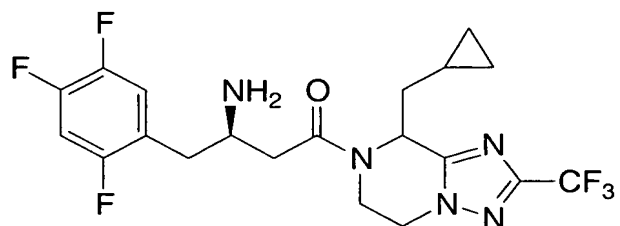
CH₂-COOCH₂Ph,
 CH₂-COOH,
 CH₂-CONMe₂, and
 CH₂OCH₃.

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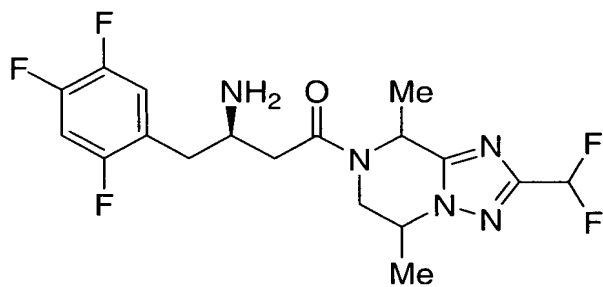
21. The compound of Claim 20 wherein R⁹ and R¹⁰ are each independently hydrogen or methyl.
22. The compound of Claim 4 which is selected from the group consisting of:



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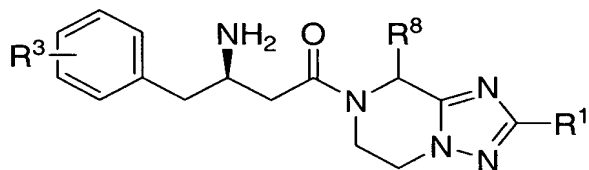


and



or a pharmaceutically acceptable salt thereof.

23. The compound of Claim 4 of the structural formula selected from the
5 group consisting of:



<u>R³</u>	<u>R⁸</u>	<u>R¹</u>
2-F,5-F	H	CF ₃
2-F,4-F,5-F	CH ₂ (4-CF ₃ -Ph)	CF ₃
2-F,4-F,5-F	CH ₂ (4-F-Ph)	CF ₃
3-F,4-F	CH ₂ (4-F-Ph)	CF ₃
3-F,4-F	CHOH(cPr)	CF ₃
2-F,4-F,5-F	H	CF ₃
2-F,4-F,5-F	CH ₂ OCH ₂ Ph	CF ₃
3-F,4-F	CH ₂ (1,2,4-triazol-1-yl)	CF ₃
2-F,4-F,5-F	CH ₂ (imidazol-	CF ₃

	1-yl)	
2-F,4-F,5-F	CH ₂ (pyrazol-1-yl)	CF ₃
2-F,5-F	Me	CF ₃
2-F,4-F,5-F	CH ₂ CO ₂ CH ₂ Ph	CF ₃
2-F,4-F,5-F	H	CHF ₂
2-F,4-F,5-F	Me	CHF ₂
2-F,4-F,5-F	CH ₂ OMe	CF ₃

24. A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

5 25. A method for inhibiting dipeptidyl peptidase-IV enzyme activity in a mammal in need thereof which comprises the administration to the mammal of an effective amount of a compound of Claim 1.

10 26. A method for treating or controlling diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

15 27. A method for treating or controlling non-insulin dependent (Type 2) diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

20 28. A method for treating or controlling hyperglycemia in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

29. A method for treating or controlling obesity in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

5 30. A method for treating or controlling one or more lipid disorders selected from the group of dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL and high LDL in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

10 31. A method for treating or controlling in a mammal in need thereof one or more conditions selected from the group consisting of (1) hyperglycemia, (2) low glucose tolerance, (3) insulin resistance, (4) obesity, (5) lipid disorders, (6) dyslipidemia, (7) hyperlipidemia, (8) hypertriglyceridemia, (9) hypercholesterolemia, (10) low HDL levels, (11) high LDL levels, (12) atherosclerosis and its sequelae, (13) vascular restenosis, (14) irritable
15 bowel syndrome, (15) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (16) other inflammatory conditions, (17) pancreatitis, (18) abdominal obesity, (19) neurodegenerative disease, (20) retinopathy, (21) nephropathy, (22) neuropathy, (23) Syndrome X, (24) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component, wherein the method comprises the administration to the
20 mammal a therapeutically effective amount of a compound of Claim 1.

32. The pharmaceutical composition of Claim 24 further comprising one or more additional active ingredients selected from the group consisting of:

- (a) a second dipeptidyl peptidase IV inhibitor;
- 25 (b) an insulin sensitizer selected from the group consisting of a PPAR γ agonist, a PPAR α/γ dual agonist, a PPAR α agonist, a biguanide, and a protein tyrosine phosphatase-1B inhibitor;
- (c) an insulin or insulin mimetic;
- (d) a sulfonylurea or other insulin secretagogue;
- 30 (e) an α -glucosidase inhibitor;
- (f) a glucagon receptor antagonist;
- (g) GLP-1, a GLP-1 mimetic, or a GLP-1 receptor agonist;
- (h) GIP, a GIP mimetic, or a GIP receptor agonist;
- (i) PACAP, a PACAP mimetic, or a PACAP receptor agonist;

(j) a cholesterol lowering agent such as (i) HMG-CoA reductase inhibitor, (ii) sequestrant, (iii) nicotiny alcohol, nicotinic acid or a salt thereof, (iv) PPAR α agonist, (v) PPAR α / γ dual agonist, (vi) inhibitor of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitor, and (viii) anti-oxidant;

- 5 (k) a PPAR δ agonist;
 (l) an antiobesity compound;
 (m) an ileal bile acid transporter inhibitor; and
 (n) an anti-inflammatory agent.

10 33. The pharmaceutical composition of Claim 32 wherein the PPAR α / γ dual agonist is KRP-297.

 34. A method of controlling or treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of
15 Claim 1 in combination with the PPAR α / γ dual agonist KRP-297.